



General

Guideline Title

Diabetes and pregnancy: an Endocrine Society clinical practice guideline.

Bibliographic Source(s)

Blumer I, Hadar E, Hadden DR, Jovanovic L, Mestman JH, Murad MH, Yegorov Y. Diabetes and pregnancy: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013 Nov;98(11):4227-49. [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [April 8, 2016 – Metformin-containing Drugs](#) : The U.S. Food and Drug Administration (FDA) is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. FDA concluded, from the review of studies published in the medical literature, that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function.

Recommendations

Major Recommendations

Definitions for the quality of the evidence (+OOO, ++OO, +++O, and ++++); the strength of the recommendation (1 or 2); and the difference between a "recommendation" and a "suggestion" are provided at the end of the "Major Recommendations" field.

Note: In this guideline, all references to diabetes specifically and exclusively refer to diabetes mellitus. Also, unless stated otherwise, the terms

diabetes, overt diabetes, and pregestational diabetes refer to either type 1 or type 2 diabetes. The Task Force uses the traditional term gestational diabetes to describe what has customarily been defined as "any degree of glucose intolerance with onset or first definition during pregnancy" while acknowledging that the more contemporary term hyperglycemia in pregnancy has strong merit as a more appropriate term. The Task Force has retained the longstanding term (gestational diabetes) owing to its widespread familiarity and traditional usage.

Preconception Care of Women with Diabetes

Preconception Counseling

The Task Force recommends that preconception counseling be provided to all women with diabetes who are considering pregnancy. (1|++OO)

Preconception Glycemic Control

The Task Force suggests that women with diabetes seeking to conceive strive to achieve blood glucose and hemoglobin A1C (HbA1C) levels as close to normal as possible when they can be safely achieved without undue hypoglycemia. (2|++OO) (See recommendations under "Glycemic Targets" below.)

Insulin Therapy

The Task Force recommends that insulin-treated women with diabetes seeking to conceive be treated with multiple daily doses of insulin or continuous subcutaneous (sc) insulin infusion in preference to split-dose, premixed insulin therapy, because the former are more likely to allow for the achievement and maintenance of target blood glucose levels preconceptionally and, in the event of pregnancy, are more likely to allow for sufficient flexibility or precise adjustment of insulin therapy. (1|++OO)

The Task Force suggests that a change to a woman's insulin regimen, particularly when she starts continuous sc insulin infusion, be undertaken well in advance of withdrawing contraceptive measures or otherwise trying to conceive to allow the patient to acquire expertise in, and the optimization of, the chosen insulin regimen. (Ungraded recommendation)

The Task Force suggests that insulin-treated women with diabetes seeking to conceive be treated with rapid-acting insulin analog therapy (with insulin aspart or insulin lispro) in preference to regular (soluble) insulin. (2|++OO)

The Task Force suggests that women with diabetes successfully using the long-acting insulin analogs insulin detemir or insulin glargine preconceptionally may continue with this therapy before and then during pregnancy. (2|++OO)

Folic Acid Supplementation

The Task Force recommends that beginning 3 months before withdrawing contraceptive measures or otherwise trying to conceive, a woman with diabetes take a daily folic acid supplement to reduce the risk of neural tube defects. (1|++OO) The Task Force suggests a daily dose of 5 mg based on this dose's theoretical benefits. (2|++OO)

Ocular Care (Preconception, during Pregnancy, and Postpartum)

The Task Force recommends that all women with diabetes who are seeking pregnancy have a detailed ocular assessment by a suitably trained and qualified eye care professional in advance of withdrawing contraceptive measures or otherwise trying to conceive (1|++++), and if retinopathy is documented, the patient should be apprised of the specific risks to her of this worsening during pregnancy. If the degree of retinopathy warrants therapy, the Task Force recommends deferring conception until the retinopathy has been treated and found to have stabilized. (1|++++)

The Task Force recommends that women with established retinopathy be seen by their eye specialist every trimester, then within 3 months of delivering, and then as needed. (1|+OOO)

The Task Force suggests that pregnant women with diabetes not known to have retinopathy have ocular assessment performed soon after conception and then periodically as indicated during pregnancy. (2|++OO)

Renal Function (Preconception and during Pregnancy)

The Task Force suggests that all women with diabetes considering pregnancy have their renal function assessed (by measuring their urine albumin to creatinine ratio, serum creatinine, and estimated glomerular filtration rate [GFR]) in advance of withdrawing contraceptive measures or otherwise trying to conceive. (Ungraded recommendation) The Task Force suggests that a woman with diabetes who has a significantly reduced GFR be assessed by a nephrologist before pregnancy, both for baseline renal assessment and to review the woman's specific risk of worsening renal function in the event of pregnancy. (Ungraded recommendation)

The Task Force suggests that all women with diabetes and preconceptional renal dysfunction have their renal function monitored regularly during pregnancy. (Ungraded recommendation)

Management of Hypertension

The Task Force recommends that satisfactory blood pressure (BP) control (<130/80 mm Hg) be achieved and maintained before withdrawing contraception or otherwise trying to conceive. (1|++OO)

The Task Force recommends that a woman with diabetes who is seeking conception while taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker in almost all cases should discontinue the medication before withdrawing contraceptive measures or otherwise trying to conceive. (1|++OO)

The Task Force suggests that in the exceptional case where the degree of renal dysfunction is severe and there is uncertainty about when conception will occur, physicians and patients be engaged in shared decision-making about whether to continue ACE inhibitors or angiotensin-receptor blockers. The patients should be informed about the possible loss of the renal protective properties if the medication is discontinued and the risk of teratogenesis if it is continued. (Ungraded recommendation)

The Task Force recommends when ACE inhibitors or angiotensin-receptor blockers have been continued up to the time of conception that the medication should be withdrawn immediately upon the confirmation of pregnancy. (1|++OO)

Elevated Vascular Risk

The Task Force recommends that if a woman with diabetes has sufficient numbers of vascular risk factors (particularly the duration of the woman's diabetes and her age), screening studies for coronary artery disease (CAD) be undertaken in advance of withdrawing contraceptive measures or otherwise trying to conceive. (1|+OOO)

The Task Force recommends that if a woman with diabetes is seeking pregnancy and has CAD, its severity should be ascertained, treatment instituted, and counseling provided as to the potential risks of pregnancy to the woman and fetus before the woman withdraws contraception or otherwise tries to conceive. (1|++++)

Management of Dyslipidemia

The Task Force recommends against the use of statins in women with diabetes who are attempting to conceive. (1|++OO)

In view of their unproven safety during pregnancy, the Task Force suggests against the routine use of fibrates and/or niacin for women with diabetes and hypertriglyceridemia attempting to conceive. (2|++OO)

The Task Force suggests that bile acid-binding resins may be used in women with diabetes to treat hypercholesterolemia; however, this is seldom warranted. (2|++OO)

Thyroid Function

For women with type 1 diabetes seeking conception, the Task Force recommends measurement of serum thyroid-stimulating hormone (TSH) and, if their thyroid peroxidase status is unknown, measurement of thyroid peroxidase antibodies before withdrawing contraceptive measures or otherwise trying to conceive. (1|+OOO)

Overweight and Obesity

The Task Force recommends weight reduction before pregnancy for overweight and obese women with diabetes. (1|+++O)

Gestational Diabetes

Testing for Overt Diabetes in Early Pregnancy

The Task Force recommends universal testing for diabetes (see Table 1 below) with a fasting plasma glucose, HbA1C, or an untimed random plasma glucose at the first prenatal visit (before 13 weeks gestation or as soon as possible thereafter) for those women not known to already have diabetes. (1|++OO) In the case of overt diabetes, but not gestational diabetes, a second test (either a fasting plasma glucose, untimed random plasma glucose, HbA1C, or oral glucose tolerance test [OGTT]) must be performed in the absence of symptoms of hyperglycemia and found to be abnormal on another day to confirm the diagnosis.

Table 1. Diagnostic Criteria for Overt Diabetes and Gestational Diabetes at the First Prenatal Visit (Before 13 Weeks Gestation or as Soon as

Possible Thereafter) for Those Women Not Known to Already Have Diabetes^a

Diagnosis	Fasting Plasma Glucose, ^b mg/dL (mmol/L)	Untimed (Random) Plasma Glucose, ^b mg/dL (mmol/L)	HbA1C, ^c %
Overt diabetes (type 1, type 2, or other)	≥126 (≥7.0)	≥200 (≥11.1)	≥6.5%
Gestational diabetes	92–125 (5.1–6.9)	NA	NA

Abbreviation: HbA1C, hemoglobin A1C; NA, not applicable.

^a These criteria for the diagnosis of overt diabetes in early pregnancy are congruent with those of the American Diabetes Association and differ somewhat from those of the International Association of the Diabetes and Pregnancy Study Groups (IADPSG).

^b Testing should use plasma glucose analyzed at a laboratory, not capillary blood glucose analyzed with a blood glucose meter.

^c Performed using a method that is certified by the NGSP (National Glycohemoglobin Standardization Program) and standardized to the Diabetes Control and Complications Trial (DCCT) reference assay.

Testing for Gestational Diabetes at 24 to 28 Weeks Gestation

The Task Force recommends that pregnant women not previously identified (either during testing performed as per recommendation "Testing for Overt Diabetes in Early Pregnancy" above or at some other time before 24 weeks gestation) with overt diabetes or gestational diabetes be tested for gestational diabetes (see Table 2 below) by having a 2-hour, 75-g OGTT performed at 24 to 28 weeks gestation. (1|+++O) The Task Force recommends that gestational diabetes be diagnosed on this test using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria (majority opinion of this committee). (1|+++O)

Table 2. Diagnostic Criteria for Overt Diabetes and Gestational Diabetes Using a 2-Hour 75-g OGTT at 24 to 28 Weeks Gestation^a

Diagnosis	Fasting Plasma Glucose, ^b mg/dL (mmol/L)	1-h Value, mg/dL (mmol/L)	2-h Value, mg/dL (mmol/L)
Overt diabetes (type 1, type 2, or other)	≥126 (≥7.0)	NA	≥200 (≥11.1)
Gestational diabetes	92–125 (5.1–6.9)	≥180 (≥10.0)	153–199 (8.5–11.0)

Abbreviation: NA, not applicable.

^a These criteria for diagnosing overt diabetes based on the results of the 24- to 28-week glucose tolerance test differ somewhat from those of the American Diabetes Association and the International Association of the Diabetes and Pregnancy Study Groups (IADPSG).

^b Testing should use plasma glucose analyzed at a laboratory, not capillary blood glucose analyzed with a blood glucose meter.

The 75-g OGTT should be performed after an overnight fast of at least 8 hours (but not more than 14 hours) and without having reduced usual carbohydrate intake for the preceding several days. The test should be performed with the patient seated, and the patient should not smoke during the test. One or more abnormal values establishes the diagnosis, with the exception that in the case of overt diabetes, but not gestational diabetes, a second test (either a fasting plasma glucose, untimed random plasma glucose, HbA1C, or OGTT), in the absence of symptoms of hyperglycemia, must be performed and found to be abnormal on another day to confirm the diagnosis of overt diabetes.

Management of Elevated Blood Glucose

The Task Force recommends that women with gestational diabetes target blood glucose levels as close to normal as possible. (1|++OO)

The Task Force recommends that the initial treatment of gestational diabetes should consist of medical nutrition therapy (see "Nutrition Therapy" below) and daily moderate exercise for 30 minutes or more. (1|+++O)

The Task Force recommends using blood glucose-lowering pharmacological therapy if lifestyle therapy is insufficient to maintain normoglycemia in

women with gestational diabetes. (1|++++)

Postpartum Care

The Task Force recommends that postpartum care for women who have had gestational diabetes should include measurement of fasting plasma glucose or fasting self-monitored blood glucose for 24 to 72 hours after delivery to rule out ongoing hyperglycemia. (1|+OOO)

The Task Force recommends that a 2-hour, 75-g OGTT should be undertaken 6 to 12 weeks after delivery in women with gestational diabetes to rule out prediabetes or diabetes. (1|+++O) If results are normal, the Task Force recommends this or other diagnostic tests for diabetes should be repeated periodically as well as before future pregnancies. (1|++OO)

The Task Force suggests the child's birth weight and whether or not the child was born to a mother with gestational diabetes become part of the child's permanent medical record. (Ungraded recommendation)

The Task Force recommends that all women who have had gestational diabetes receive counseling on lifestyle measures to reduce the risk of type 2 diabetes, the need for future pregnancies to be planned, and the need for regular diabetes screening, especially before any future pregnancies. (1|+OOO)

The Task Force suggests blood glucose-lowering medication should be discontinued immediately after delivery for women with gestational diabetes unless overt diabetes is suspected, in which case the decision to continue such medication should be made on a case-by-case basis. (2|++OO)

Glucose Monitoring and Glycemic Targets

Self-Monitoring of Blood Glucose

The Task Force recommends self-monitoring of blood glucose in all pregnant women with gestational or overt diabetes (1|++++) and suggests testing before and either 1 or 2 hours after the start of each meal (choosing the postmeal time when it is estimated that peak postprandial blood glucose is most likely to occur) and, as indicated, at bedtime and during the night. (2|++OO)

Glycemic Targets

Table 3. Glycemic Targets Preconceptionally for Women with Overt Diabetes and during Pregnancy for Women with Either Overt Diabetes or Gestational Diabetes^a

	Target Value, mg/dL (mmol/L)
Preprandial blood glucose	≤95 (5.3) ^b
1 h after the start of a meal	≤140 (7.8)
2 h after the start of a meal	≤120 (6.7)

^a Note that blood glucose meters use capillary blood but display corrected results equivalent to plasma glucose levels.

^b Target fasting blood glucose is ≤90 (5.0 mmol/L) if this can be safely achieved without undue hypoglycemia.

The Task Force recommends pregnant women with overt or gestational diabetes strive to achieve a target preprandial blood glucose <95 mg/dL (5.3 mmol/L). (1|++OO for fasting target, 1|+OOO for other meals).

The Task Force suggests that an even lower fasting blood glucose target of <90 mg/dL (5.0 mmol/L) be strived for (2|+OOO) if this can be safely achieved without undue hypoglycemia.

The Task Force suggests pregnant women with overt or gestational diabetes strive to achieve target blood glucose levels 1 hour after the start of a meal <140 mg/dL (7.8 mmol/L) and 2 hours after the start of a meal <120 mg/dL (6.7 mmol/L) (2|+OOO) when these targets can be safely achieved without undue hypoglycemia.

The Task Force suggests pregnant women with overt diabetes strive to achieve a HbA1C <7% (ideally <6.5%). (2|+OOO)

Continuous Glucose Monitoring

The Task Force suggests that continuous glucose monitoring be used during pregnancy in women with overt or gestational diabetes when self-monitored blood glucose levels (or, in the case of the woman with overt diabetes, HbA1C values) are not sufficient to assess glycemic control (including both hyperglycemia and hypoglycemia). (2|++OO)

Nutrition Therapy and Weight Gain Targets for Women with Overt or Gestational Diabetes

Nutrition Therapy

The Task Force recommends medical nutrition therapy for all pregnant women with overt or gestational diabetes to help achieve and maintain desired glycemic control while providing essential nutrient requirements. (1|++OO)

Weight Management

The Task Force suggests that women with overt or gestational diabetes follow the Institute of Medicine revised guidelines for weight gain during pregnancy (See Table 4 below). (Ungraded recommendation)

Table 4. 2009 Institute of Medicine Recommendations for Total Weight Gain and Rate of Weight Gain during Pregnancy, by Prepregnancy Body Mass Index (BMI)

Pregpregnancy BMI	Total Weight Gain		Rates of Weight Gain in Second and Third Trimester ^a	
	Range, kg	Range, lb	Mean (Range), kg/wk	Mean (Range), lb/wk
Underweight (<18.5 kg/m ²)	12.5–18	28–40	0.51 (0.44–0.58)	1 (1–1.3)
Normal weight (18.5–24.9 kg/m ²)	11.5–16	25–35	0.42 (0.35–0.50)	1 (0.8–1)
Overweight (25.0–29.9 kg/m ²)	7–11.5	15–25	0.28 (0.23–0.33)	0.6 (0.5–0.7)
Obese (≥30.0 kg/m ²)	5–9	11–20	0.22 (0.17–0.27)	0.5 (0.4–0.6)

^a Calculations assume a 0.5- to 2-kg (1.1–4.4 lb) weight gain in the first trimester.

The Task Force suggests obese women with overt or gestational diabetes reduce their calorie intake by approximately one-third (compared with their usual intake before pregnancy) while maintaining a minimum intake of 1600 to 1800 kcal/d. (2|++OO)

Carbohydrate Intake

The Task Force suggests women with overt or gestational diabetes limit carbohydrate intake to 35% to 45% of total calories, distributed in 3 small- to moderate-sized meals and 2 to 4 snacks including an evening snack. (2|++OO)

Nutritional Supplements

The Task Force recommends pregnant women with overt or gestational diabetes should follow the same guidelines for the intake of minerals and vitamins as for women without diabetes (1|++OO), with the exception of taking folic acid 5 mg daily beginning 3 months before withdrawing contraceptive measures or otherwise trying to conceive (see recommendation under "Folic Acid Supplementation" above). The Task Force suggests that at 12 weeks gestation, the dose of folic acid be reduced to 0.4 to 1.0 mg/d, which should be continued until the completion of breastfeeding. (2|++OO)

Blood Glucose-Lowering Pharmacological Therapy during Pregnancy

Insulin Therapy

The Task Force suggests that the long-acting insulin analog detemir may be initiated during pregnancy for those women who require basal insulin and for whom neutral protamine Hagedorn (NPH) insulin, in appropriate doses, has previously resulted in, or for whom it is thought NPH insulin may result in, problematic hypoglycemia; insulin detemir may be continued in those women with diabetes already successfully taking insulin detemir before pregnancy. (2|++++)

The Task Force suggests that those pregnant women successfully using insulin glargine before pregnancy may continue it during pregnancy.

(2|++OO)

The Task Force suggests that the rapid-acting insulin analogs lispro and aspart be used in preference to regular (soluble) insulin in pregnant women with diabetes. (2|+++O)

The Task Force recommends the ongoing use of continuous sc insulin infusion during pregnancy in women with diabetes when this has been initiated before pregnancy (1|+++O), but suggest that continuous sc insulin infusion not be initiated during pregnancy unless other insulin strategies including multiple daily doses of insulin have first been tried and proven unsuccessful. (2|++OO)

Noninsulin Antihyperglycemic Agent Therapy

The Task Force suggests that glyburide (glibenclamide) is a suitable alternative to insulin therapy for glycemic control in women with gestational diabetes who fail to achieve sufficient glycemic control after a 1-week trial of medical nutrition therapy and exercise except for those women with a diagnosis of gestational diabetes before 25 weeks gestation and for those women with fasting plasma glucose levels >110 mg/dL (6.1 mmol/L), in which case insulin therapy is preferred. (2|++OO)

The Task Force suggests that metformin therapy be used for glycemic control only for those women with gestational diabetes who do not have satisfactory glycemic control despite medical nutrition therapy and who refuse or cannot use insulin or glyburide and are not in the first trimester. (2|++OO)

Labor, Delivery, Lactation, and Postpartum Care

Blood Glucose Targets during Labor and Delivery

The Task Force suggests target blood glucose levels of 72 to 126 mg/dL (4.0 to 7.0 mmol/L) during labor and delivery for pregnant women with overt or gestational diabetes. (2|++OO)

Lactation

The Task Force recommends whenever possible women with overt or gestational diabetes should breastfeed their infant. (1|++++)

The Task Force recommends that breastfeeding women with overt diabetes successfully using metformin or glyburide therapy during pregnancy should continue to use these medications, when necessary, during breastfeeding. (1|++++)

Postpartum Contraception

The Task Force recommends that the choice of a contraceptive method for a woman with overt diabetes or a history of gestational diabetes should not be influenced by virtue of having overt diabetes or a history of gestational diabetes. (1|+++O)

Screening for Postpartum Thyroiditis

The Task Force suggests that women with type 1 diabetes be screened for postpartum thyroiditis with a TSH at 3 and 6 months postpartum. (2|++OO)

Definitions:

Quality of Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

Strength of Recommendation

1 - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

Ungraded. The panelists on a few occasions left some recommendations ungraded. These are recommendations that were supported only by

indirect evidence or by the unsystematic observations of the committee members and resulted from their consensus and discussion and have been included owing to their clinical relevance and practicality. These recommendations should be considered suggestions (i.e., deviation from these recommendations is not unreasonable) and are explicitly left ungraded due to the lack of direct evidence.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Diabetes mellitus (type 1 or type 2) during preconception, pregnancy, and postpartum
- Gestational diabetes

Guideline Category

Counseling

Diagnosis

Management

Screening

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Nutrition

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Dietitians

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To formulate a clinical practice guideline for the management of the pregnant woman with diabetes

Target Population

- Patients with diabetes during preconception, pregnancy, and postpartum
- Pregnant women without known pre-existing diabetes

Interventions and Practices Considered

1. Preconception care of women with diabetes
 - Preconception counseling
 - Preconception glycemic control (blood glucose and hemoglobin A1C [HbA1C] levels as close to normal as possible)
 - Insulin therapy
 - Folic acid supplementation
 - Ocular care (preconception, during pregnancy, and postpartum)
 - Renal function assessment (preconception and during pregnancy)
 - Management of hypertension (achieving blood pressure control [$<130/80$ mm Hg], discontinuing angiotensin-converting enzyme [ACE] inhibitor or angiotensin-receptor blocker therapy before trying to conceive)
 - Screening studies for coronary artery disease and treatment as indicated
 - Management of dyslipidemia (avoiding statins and routine use of fibrates and/or niacin for women attempting to conceive)
 - Thyroid function tests (measurement of serum thyroid-stimulating hormone [TSH] and thyroid peroxidase)
 - Weight reduction before pregnancy for overweight and obese women
2. Management of gestational diabetes
 - Universal testing for diabetes in early pregnancy with a fasting plasma glucose, HbA1C, or an untimed random plasma glucose
 - Testing for gestational diabetes at 24 to 28 weeks gestation using a 2-hour, 75-g oral glucose tolerance test (OGTT)
 - Management of elevated blood glucose
 - Postpartum care
3. Glucose monitoring and glycemic targets
 - Self-monitoring of blood glucose
 - Establishing target blood glucose levels
 - Continuous glucose monitoring
4. Nutrition therapy and weight gain targets for women with overt or gestational diabetes
 - Medical nutrition therapy
 - Weight management and rates of weight gain during pregnancy
 - Calorie reduction in obese women
 - Limiting carbohydrate intake
 - Use of nutritional supplements
5. Blood glucose-lowering pharmacological therapy during pregnancy
 - Insulin therapy (long-acting insulin analog detemir, insulin glargine, neutral protamine Hagedorn [NPH] insulin, rapid-acting insulin analogs lispro and aspart in preference to regular [soluble] insulin, ongoing use of continuous subcutaneous [sc] insulin infusion during pregnancy)
 - Noninsulin antihyperglycemic agent therapy (glyburide [glibenclamide], metformin)
6. Labor, delivery, lactation, and postpartum care
 - Blood glucose targets during labor and delivery
 - Breastfeeding
 - Medication use during breastfeeding
 - Choice of postpartum contraception
 - Screening for postpartum thyroiditis

Major Outcomes Considered

- Sensitivity and specificity for 1-hour 50-g glucose challenge test
- Glycemic control (attainment of postprandial blood glucose target)
- Maternal and fetal outcomes, including rates of congenital anomalies and spontaneous abortions, frequency of macrosomia, admission to neonatal intensive care, other perinatal morbidity, and mortality

- Rates of maternal and neonatal hypoglycemia
- Risk of neural tube defects
- Risks of retinopathy, renal dysfunction, hypertension, and preeclampsia during pregnancy
- Risk for the later development of impaired fasting glucose, impaired glucose tolerance, overt diabetes, and the metabolic syndrome in women who have had gestational diabetes
- Risk for complications during pregnancy (including hypertensive complications, stillbirth, and increased risk for cesarean section) in women who are overweight or obese before pregnancy
- Risk for developing thyroiditis

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The Endocrine Society's Task Force commissioned two systematic reviews (see the "Availability of Companion Documents" field) and used the best available research evidence to develop the guideline recommendations.

Glucose Targets in Pregnant Women with Diabetes: A Systematic Review and Meta-Analysis

Eligibility Criteria

The Task Force included randomized controlled trials (RCTs) and observational studies that enrolled pregnant women with type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM) in pregnancy and evaluated the association between different blood glucose targets achieved during pregnancy and maternal and fetal outcomes.

Search Methods

An expert reference librarian, following the protocol, designed and conducted electronic search strategies (see Supplemental Table 1, published on [The Endocrine Society's Journals Online website](#)) with input from study investigators with expertise in conducting systematic reviews. Electronic databases Medline, EMBASE and Cochrane Library (through the OVID interface), Web of Science, Scopus, PsycINFO, and CINAHL, from inception through May 2011 were searched. To identify additional candidate studies, 2 reviewers reviewed the reference lists of the eligible primary studies, narrative reviews, and systematic reviews and queried experts.

Selection of Studies

Two reviewers working independently considered the potential eligibility of each of the abstracts and titles that resulted from the search strategy. Disagreements in the abstract and title screening were automatically considered eligible for the full text review. Eligible studies were reviewed in full text versions (all available versions of each study). Substantial agreement ($\kappa=0.80$) was achieved during full text screening phase.

Screening for Gestational Diabetes: A Systematic Review and Meta-Analysis

Eligibility Criteria

RCTs and observational studies that enrolled pregnant woman of any age who were screened for GDM were included.

Search Methods

An expert reference librarian designed and conducted an electronic search strategy (see Supplemental Table 6, published on [The Endocrine Society's Journals Online website](#)) with input from study investigators with expertise in conducting systematic reviews. Electronic databases were searched to identify relevant studies (Ovid Medline, OVID EMBASE, OVID Cochrane Library, Web of Science,

Scopus, PsycINFO, and CINAHL) from November 2007 through May 2011. References published before this date were also obtained. To identify additional candidate studies, the reference lists of the eligible primary studies, narrative reviews, and systematic reviews were reviewed; and the expert members of the commissioning task force were queried.

Selection of Studies

Two reviewers working independently considered the potential eligibility of each of the abstracts and titles that result from executing the search strategy. All the available versions of the eligible studies were reviewed in full-text versions. Agreement for inclusion was measured by inter-reviewer agreement beyond chance (kappa-coefficient).

Number of Source Documents

Glucose Targets in Pregnant Women with Diabetes: A Systematic Review and Meta-Analysis

The literature search identified 1536 potentially eligible citations, of which 34 original studies met the eligibility criteria (15 randomized controlled trials, 18 cohort studies, and 1 case-control study). No unpublished studies were identified.

Screening for Gestational Diabetes: A Systematic Review and Meta-Analysis

A literature search identified 915 articles of which 39 original studies in 42 publications met the eligibility criteria and were included in the systematic review.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

Methods Used to Analyze the Evidence

Meta-Analysis

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The Endocrine Society's Task Force commissioned two systematic reviews (see the "Availability of Companion Documents" field) and used the best available research evidence to develop the guideline recommendations.

[Glucose Targets in Pregnant Women with Diabetes: A Systematic Review and Meta-Analysis: Attached](#)

Data Extraction and Management

Using a standardized, piloted, and web-based data extraction form and working in duplicates, the following descriptive data was abstracted from each study: full description of participants enrolled (e.g., age, ethnicity, and type of diabetes), interventions received, monitoring for efficacy and for adherence to the treatment, outcomes, and source of funding. The outcomes of interest were 1) macrosomia (birth weight ≥ 4000 g); 2) other fetal outcomes such as large for gestational age (LGA), neonatal mortality, brachial plexus injury, clavicular fracture, admission to a neonatal intensive care unit (ICU), hypoglycemia requiring treatment, hyperbilirubinemia requiring treatment or admission to an ICU, and respiratory distress syndrome; and 3) maternal outcomes such as maternal mortality, preeclampsia, and gestational hypertension.

Author Contact

When data were not available or unclear from the published papers, repeated efforts were performed to contact the authors. The reviewers contacted the corresponding author of each study twice within 2 weeks via email or, when email was not available, by phone or mail. After author contact, studies with data insufficient for analysis were excluded.

Assessment of Risk of Bias in Included Studies

To assess the methodological quality of the included randomized controlled trials (RCTs) the Cochrane Collaboration's Risk of Bias assessment tool was used to evaluate randomization performance and methods, allocation concealment, baseline imbalances, extent of blinding (patients, caregivers, data collectors, outcome assessors, and data analysts), rate of loss to follow-up, and monitoring of adherence to the follow-up and its efficiency. For the observational studies, the Newcastle-Ottawa scale was used to evaluate how the groups were selected, the comparability between them, whether there was adequate follow-up, and how outcomes/exposures were ascertained.

Statistical Analysis

The effect size as odds ratio (OR) and 95% confidence interval (CI) across the included studies were pooled. The Der-Simonian and Laird random-effects methods were adopted, whereas the heterogeneity was estimated using the Mantel-Haenszel model. Random-effects meta-regression models were constructed after adjusting for diabetes type, trimester, diabetes treatment, and body mass index (BMI), whenever possible.

Heterogeneity across individual studies was assessed using the Cochran's Q statistical test. A more conservative criterion of $P < .10$ was adopted to suggest heterogeneity. Plans were to assess for publication bias using the Egger regression asymmetry test and visual inspection using funnel plots. However, evaluation of publication bias was not feasible due to significant heterogeneity between the included studies. The possibility of reporting bias was explored by assessing the proportion of studies reporting the levels of exposure (target glucose level) and outcomes of interest of the overall number of studies; a low proportion suggests reporting bias. All meta-analyses were conducted using STATA version 12 software (StataCorp).

Subgroups Analysis

Several a priori hypotheses were determined to explore subgroup interactions and give a potential explanation for heterogeneity. Subgroup analysis was based on diabetes type (type 1, type 2, or gestational diabetes) and trimester (first, second, or third). Plans were to conduct a test of interaction to evaluate the significance of subgroup analyses and potential correlation between subgroups and the pooled effect size.

Screening for Gestational Diabetes: A Systematic Review and Meta-Analysis

Data Extraction and Management

Using a standardized, piloted, and web-based data extraction form and working in duplicates, the following descriptive data were abstracted from each study: full description of participants enrolled (principal baseline characteristics such as age, ethnicity, and risk factors), the screening test they received, the outcomes of interest, and the source of funding. The outcomes of interest for this review were 1) screening yield (proportion of women with a positive screening results), 2) sensitivity/specificity of the test, 3) maternal outcomes (maternal mortality, preeclampsia, or gestational hypertension), and 4) fetal outcomes (neonatal mortality, brachial plexus injury, clavicle fracture, admission to a neonatal intensive care unit, neonatal hypoglycemia, neonatal hyperbilirubinemia, respiratory distress syndrome, and macrosomia). Additionally, the population of each study was classified according to the baseline risk for developing gestational diabetes mellitus as 1 of 3 categories (high, average, and low-risk).

Author Contact

The reviewers planned to contact the authors of original studies by email when data were not available from the published papers or required clarification (with a repeat e-mail in 2 weeks if no response). They were able to contact only one author for successful clarification. After author contact, studies with data insufficient for analysis were excluded.

Assessment of Risk of Bias in Included Studies

To assess the methodological quality of the included RCTs, the Cochrane risk of bias assessment tool was used to evaluate randomization performance and methods, allocation concealment, baseline imbalances, extent of blinding (patients, caregivers, data collectors, outcome assessors, and data analysts), and rate of loss to follow-up. For the observational studies, the Newcastle-Ottawa scale was used to evaluate how the groups were selected, the comparability between them, whether there was adequate follow-up, and how outcomes/exposures were ascertained.

Meta-Analysis

This systematic review included dichotomous outcomes; therefore, the effect size was measured using the OR and 95% CI. The I^2 statistic was used to measure inconsistency in results across and within the studies that was not attributable to chance. To pool data across studies, the random-effect models was used because it provides a more reliable estimate of the variance between studies when the number of included studies is small. Analyses were performed using Comprehensive Meta-Analysis (CMA) version 2.2 (Biostat Inc).

Assessment of Publication Bias

Plans were to evaluate for publication bias by visually inspecting funnel plots and conducting statistical testing for plot symmetry using the Egger test. However, the assumptions of publication bias testing require a large number (>20) of homogeneous studies.

Subgroup Analysis, Meta-regression, and Sensitivity Analysis

A priori hypotheses (limited to a small number to avoid chance findings) were determined to explore subgroup interactions and give a potential explanation for heterogeneity. Subgroup analyses were based on 1) timing of screening in pregnancy, 2) modality of screening, and 3) time of day for glucose tolerance test (morning vs afternoon).

Plans were to conduct a test of interaction to evaluate the significance of subgroup analyses and potential correlation between subgroups and the pooled effect size. A meta-regression was conducted to assess the correlation between the glucose value obtained in the screening test (independent variable) and the development of the outcomes previously mentioned (dependent variable).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Participants

The Task Force was composed of a chair, selected by the Clinical Guidelines Subcommittee of the Endocrine Society, 5 additional experts, a methodologist, and a medical writer.

Evidence

This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to describe both the strength of recommendations and the quality of evidence.

Consensus Process

One group meeting, several conference calls, and innumerable e-mail communications enabled consensus for all recommendations save one with a majority decision being employed for this single exception.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

1 - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

Ungraded. The panelists on a few occasions left some recommendations ungraded. These are recommendations that were supported only by indirect evidence or by the unsystematic observations of the committee members and resulted from their consensus and discussion and have been included owing to their clinical relevance and practicality. These recommendations should be considered suggestions (i.e., deviation from these recommendations is not unreasonable) and are explicitly left ungraded due to the lack of direct evidence.

Cost Analysis

A cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The Endocrine Society Clinical Guidelines Subcommittee and Clinical Affairs Core Committee provided careful critical review of earlier versions of the manuscript as well as helpful comments and suggestions. The members of the Endocrine Society kindly reviewed the draft version of the manuscript when it was posted on the Society's website and sent additional comments and suggestions. External peer review was performed by the journal prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate preconception counseling and management of women with diabetes mellitus during pregnancy and postpartum

Potential Harms

- Continuous subcutaneous (SC) insulin has been reported to cause an increased risk of maternal ketoacidosis and neonatal hypoglycemia.
- The Task Force acknowledges that with universal testing for diabetes in early pregnancy, there will be a high rate of false-positive results and that women with positive testing may have anxiety and will suffer the burden of additional testing. Nevertheless, we recommended universal testing because we place the highest value on preventing fetal complications.

Qualifying Statements

Qualifying Statements

- Clinical Practice Guidelines are developed to be of assistance to endocrinologists and other health care professionals by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all proper approaches or

methods, or exclusive of others. The Guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of health care providers and each patient's individual circumstances.

- The Endocrine Society makes no warranty, express or implied, regarding the Guidelines and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. The Society shall not be liable for direct, indirect, special, incidental, or consequential damages related to the use of the information contained herein.
- This guideline advocates for use of best practices based on an analysis of the contemporary (and older) medical literature. It is, however, recognized that cost considerations and other practical realities may not necessarily allow for implementation of certain recommendations in some locales.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Blumer I, Hadar E, Hadden DR, Jovanovic L, Mestman JH, Murad MH, Yegorov Y. Diabetes and pregnancy: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2013 Nov;98(11):4227-49. [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Nov

Guideline Developer(s)

The Endocrine Society - Professional Association

Source(s) of Funding

The Endocrine Society

Guideline Committee

The Diabetes and Pregnancy Guidelines Task Force

Composition of Group That Authored the Guideline

Task Force Members: Ian Blumer (*Chair*), Eran Hadar, David R. Hadden, Lois Jovanovic, Jorge H. Mestman, M. Hassan Murad, and Yariv Yogev

Financial Disclosures/Conflicts of Interest

The Endocrine Society maintains a rigorous conflict of interest review process for the development of clinical practice guidelines. All Task Force members must declare any potential conflicts of interest, which are reviewed before they are approved to serve on the Task Force and periodically during the development of the guideline. The conflict of interest forms are vetted by the Clinical Guidelines Subcommittee (CGS) before the members are approved by the Society's Council to participate on the guideline Task Force. Participants in the guideline development must include a majority of individuals without conflict of interest in the matter under study. Participants with conflicts of interest may participate in the development of the guideline, but they must have disclosed all conflicts. The CGS and the Task Force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined by remuneration in any amount from the commercial interest(s) in the form of grants; research support; consulting fees; salary; ownership interest (e.g., stocks, stock options, or ownership interest excluding diversified mutual funds); honoraria or other payments for participation in speakers' bureaus, advisory boards, or boards of directors; or other financial benefits. Completed forms are available through the Endocrine Society office.

Financial Disclosure of Task Force

Ian Blumer, MD (*Chair*) is a speaker for Astra-Zeneca, Bristol Myers Squibb, Eli Lilly, Medtronic, Novo Nordisk, Roche and Sanofi-Aventis. He is also a member of advisory board for Bayer, Eli Lilly, GlaxoSmithKline, Novo Nordisk, Janssen Pharmaceuticals, and Takeda.

David R. Hadden, MD is a member of the data monitoring committee for Novo Nordisk and a technical editor for Wiley-Blackwell Publishing.

M. Hassan Murad, MD, Lois Jovanovic, MD, Jorge H. Mestman, MD, Eran Hadar, MD and Yariv Yogev, MD have no relevant financial relationships to declare.

Guideline Endorser(s)

American Diabetes Association - Professional Association

European Society of Endocrinology - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from [The Endocrine Society Web site](#) .

Print copies: Available from The Endocrine Society, Phone: (301) 941.0210; Email: Societyservices@endo-society.org

Availability of Companion Documents

The following are available:

- Prutsky GJ, Domecq JP, Wang Z, Carranza Leon BG, Elraiyah T, Nabhan M, Sundaresh V, Vella A, Montori VM, Murad MH. Glucose targets in pregnant women with diabetes: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2013 Nov;98(11):4319-24. Electronic copies: Available to subscribers from the [Journal of Clinical Endocrinology & Metabolism \(JCEM\) Web site](#) .
- Prutsky GJ, Domecq JP, Sundaresh V, Elraiyah T, Nabhan M, Prokop, LJ, Vella A, Montori VM, Murad MH. Screening for gestational diabetes: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2013 Nov;98(11):4311-18. Electronic copies: Available to subscribers from the [JCEM Web site](#) .

In addition, continuing medical education activities are available in the [original guideline document](#) .

Print copies: Available from The Endocrine Society, Phone: (301) 941.0210; Email: Societyservices@endo-society.org

Patient Resources

The following is available:

- Diabetes and pregnancy. A patient's guide. Hormone Health Network. 2014 Feb. 2 p. Electronic copies: Available from the [Hormone Health Network Web site](#) .

A variety of fact sheets (English and Spanish) and patient guides (English) are available from the [Hormone Health Network Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on July 7, 2014. The information was verified by the guideline developer on July 16, 2014. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-

containing Drugs.

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